

## Communicable Disease Prevention and Epidemiology

Health Advisory - October 27, 2001

## **Update on Diagnosis and Management of Anthrax**

## Reporting suspected anthrax cases to Public Health

Any previously healthy patient with the following clinical presentations should be immediately reported to Public Health at 206-296-4774 (24 hours)

Note: this procedure is applicable to health providers in King County, Washington State only:

- Severe, unexplained febrile illness or death
- Sepsis or respiratory failure with a widened mediastinum
- Sepsis with gram-positive rods or a suspicious Bacillus species identified in the blood or cerebrospinal fluid
- All suspected cases of anthrax

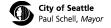
## **Cutaneous anthrax: Treatment and prophylaxis recommendations**

Cutaneous anthrax usually begins as a small papule, enlarges, and progresses to a vesicle or bulla in 1-2 days. The vesicle may become hemorrhagic, with satellite vesicles. The lesion then ulcerates and forms a black eschar (necrotic ulcer) in 3 to 7 days. The lesion is usually painless and the tissue surrounding the skin lesion is often erythematous, and may have varying degrees of edema (brawny, gelatinous, non-pitting edema). Patients may have fever, malaise, headache and regional lymphadenopathy. The case fatality rate for cutaneous anthrax is 20% without, and <1% with, antibiotic treatment. Cutaneous anthrax is not easily transmissible from person to person, although there is a very low risk of infection if there is direct contact with the drainage from an open sore. The incubation period is usually from 1-7 days (range 1-12 days).

#### See Tables at end of document for treatment and prophylaxis recommendations.

Public Health requests that clinicians report any patients with a skin lesion suspicious for cutaneous anthrax or a concerning skin lesion even if it does not fit the classical description, if any one of the following are present:

- 1. a history of working in or having visited a major media establishment, particularly if the patient handles mail: OR
- 2. the patient is employed as a mail handler; OR
- 3. a history of exposure to a threatening letter with powder; OR
- 4. laboratory evidence suggestive of possible *B. anthracis* infection (including Gram positive bacilli on Gram stain from a skin lesion, sterile fluid, or tissue, or encapsulated non-motile non-hemolytic bacilli on culture from any body fluid or site)





For patients meeting these criteria, Public Health can assist clinicians in obtaining appropriate diagnostic specimens.

## Inhalational or meningeal anthrax

There have been no cases of anthrax in Washington State. However, recent events emphasize the need for clinicians to maintain vigilance regarding any unusual disease clusters or manifestations that might represent an intentional outbreak, particularly among mail handlers at this time.

Inhalational anthrax usually presents as a brief prodrome resembling a viral respiratory illness followed by development of hypoxia and dyspnea, with radiographic evidence of mediastinal widening. Pleural effusions may be present, focal infiltrates are not typically seen but can occur. CT scans on some cases have shown mediastinal lymphadenopathy and pleural effusions. The incubation period of inhalational anthrax is reported to be typically between 1 and 7 days (range possibly up to 60 days). Initial symptoms include fever, dyspnea, cough, headache, muscle aches and malaise. Two recent cases also had GI symptoms including nausea, vomiting and diarrhea. These symptoms may progress to respiratory failure and shock. Meningitis frequently develops, and the spinal fluid may be hemorrhagic. Case-fatality rates are extremely high, even when appropriate antibiotics are administered. Early treatment in the prodromal stage is much more effective in preventing severe illness and death. Appropriate clinical specimens for diagnosing inhalational anthrax include blood, (Gram stain may be positive on unspun blood in advanced disease), pleural fluid, and if meningeal signs are present, CSF.

See Tables at end of document for treatment and prophylaxis recommendations.

## Avoid prescribing unnecessary antibiotics

Public Health recommends physicians NOT prescribe prophylactic antibiotics for the general public. There have been no cases of anthrax in our area. Prophylactic antibiotics should be limited to persons with a known exposure to anthrax or a credible threat as determined after a law enforcement investigation in consultation with Public Health. Clinicians seeing patients who report they may have been exposed to anthrax should see **Risk assessment and response to possible anthrax exposures for clinicians below**.

#### Anthrax vaccines are not commercially available or recommended

There is currently no indication for the use of anthrax vaccine. At this time, anthrax vaccine is in limited supply and only available for military personnel at risk for potential exposure to anthrax in combat settings. Anthrax vaccine is not available to the general public or the medical community. Anthrax vaccination currently requires 6 shots over an 18-month period with periodic boosters.

## There is NO role for nasal swab testing in clinical decision-making

There is no screening test available for the detection of anthrax infection in asymptomatic persons. Public Health discourages the use of nasal swabs for assessing patients concerned about exposure to anthrax. A negative nasal swab result does not rule-out anthrax exposure. Decisions regarding administration of antibiotic prophylaxis for anthrax should be made based upon the risk of exposure, not the results of nasal swab testing.

Nasal swab testing for anthrax spores is used in epidemiologic investigations of persons with a known exposure to anthrax or to a credible threat as determined after a law enforcement

investigation in consultation with Public Health. The results are used to guide further investigation and to determine the source and extent of exposure in a population, not to determine which individuals should be given preventive therapy. The sensitivity and specificity and clinical value of nasal swab testing are unknown.

## **Cutaneous anthrax: Clinical evaluation guidelines**

A highly suspicious case of cutaneous anthrax is any person with a suspicious skin lesion meeting the following clinical criteria:

- An ulcerative lesion with surrounding erythema, edema or vesicles AND/OR a blackened eschar
- 2. Any person with a less suspicious skin lesion (an ulcerative or necrotic lesion), with any of the following:
  - a) a history of working in or having visited a major media establishment, particularly if the patient handles mail; OR
  - b) is employed as a mail handler; OR
  - c) a history of exposure to a threatening letter with powder, OR
  - d) laboratory evidence suggestive of possible *B. anthracis* infection (including Gram positive bacilli on Gram stain from a skin lesion, sterile fluid, or tissue, or encapsulated non-motile non-hemolytic bacilli on culture from any bodily fluid or site)

Instructions for collecting diagnostic specimens for suspected cases of cutaneous anthrax:

For highly suspicious cases consult with Public Health immediately (206-296-4774, 24 hours), preferably before obtaining specimens. Public Health will facilitate transport of specimens to the WA State PHL and CDC. Recommended specimens include:

- 1. Two skin biopsies for PCR, culture and immunohistochemical staining at CDC:
  - a) One biopsy specimen in formalin (keep at room temperature) for histopathology and immunohistochemical staining. Paraffin-embedded specimens are acceptable as well.
  - b) One biopsy specimen in a sterile cup (freeze at -70° C or place on dry ice) for culture and PCR.
  - c) If only one biopsy is obtained, it should be fresh frozen and not placed in formalin.
- 2. Culture and Gram stain of skin lesion or skin biopsy for testing at your clinical microbiology laboratory:
  - a) Synthetic (non-cotton) swab with non-wooden stick for culture and gram stain of material swabbed from the exudate or the most actively inflammed area of the eschar.
  - b) Sterile punch biopsy specimen should be sent in sterile saline for culture.
  - c) Send to routine hospital laboratory; if suspicious bacillus species\* is identified, contact Public Health immediately.
- 3. Acute serum for ELISA testing for *B. anthracis* at CDC (Ideally, within 5 days of illness onset):
  - a) Collect ~5 ml of whole blood in a serum separator tube, refrigerate or keep at room air.
  - b) Spin down as soon as possible.
  - c) After spinning, separate serum and freeze the tube of serum at -70° C or place on dry ice.

- 4. Convalescent serum for ELISA testing for *B. anthracis* at CDC (14-21 days after acute sera):
  - a) Collect ~5 ml of whole blood in a serum separator tube, refrigerate or keep at room air.
  - b) Spin down as soon as possible.
  - c) After spinning, separate serum and freeze the tube of serum at -70° C or place on dry ice.
- 5. If the patient is febrile or hospitalized, please also collect:
  - a) Blood culture: send to hospital clinical laboratory; if suspicious bacillus species\* is identified, contact Public Health immediately.
  - b) Whole blood for PCR EDTA containing tube (purple top)
- » Less suspicious cases of cutaneous anthrax are persons with skin lesions including:
- 1. Patients with skin lesions in which cutaneous anthrax is part of the differential diagnosis, but in which the clinician does not strongly suspect it, and:
  - a) no potential exposure has occurred, and
  - b) there is no laboratory evidence of infection with a bacillus species.
- » For less suspicious cases providers may wish to obtain the following specimens:
- 1. Culture and gram stain of skin lesion:
  - a) Synthetic (non-cotton) swab with non-wooden stick for culture and gram stain of material swabbed from the exudate or the most actively inflammed area of the eschar.
  - b) Sterile punch biopsy specimen should be sent in sterile saline for culture.
  - c) Send to your routine hospital laboratory; if suspicious *bacillus species\** is identified, contact Public Health immediately.
- 2. Blood culture (if patient is hospitalized, febrile, toxic, or skin lesion is severely erythematous or edematous):
  - a) Send to your routine hospital laboratory; if suspicious *bacillus species\** is identified, contact Public Health immediately.
- » Please be sure to completely and clearly label all specimens with the following information:
- PATIENT'S FIRST AND LAST NAME
- DATE OF BIRTH
- DATE OF COLLECTION OF SPECIMEN
- SITE OF SPECIMEN COLLECTION
- RULE-OUT ANTHRAX
- PHYSICIAN NAME AND CONTACT NUMBER
- \* Suspicious Bacillus species: large, Gram positive rods with spores; non-motile and non-hemolytic.

## Important information on anthrax for clinical microbiologists

Clinical microbiology laboratories should take care not to regard all isolates of Bacillus species as contaminants, especially if isolated from sterile sites (blood, cerebrospinal fluid) and/or multiple cultures are positive from the same patient. Public Health recommends that all sterile site Bacillus isolates be further evaluated. If non-motile or non-hemolytic, and/or if the clinical syndrome is suggestive of anthrax, contact Public Health immediately at 206-296-4774 (24 hours) and refer the isolates immediately to the WA State Public Health Laboratory (PHL) for further testing (Public Health can facilitate transport of isolates to the PHL).

## » Laboratory issues with respect to diagnosing *Bacillus anthracis* include:

- Bacillus anthracis can be isolated primarily from blood, sputum, CSF, vesicular fluid, a swab of exudate from the eschar, a tissue biopsy and stool (if gastrointestinal anthrax).
- Clinical laboratory specimens should be handled in Biosafety Level 2 facilities.
- Confirmatory diagnostic testing is available through the WA State PHL; positive specimens would be sent to the CDC for additional testing.

## » Presumptive identification key for Bacillus anthracis:

- Non-hemolytic
- Non-motile
- Encapsulated (requires India ink to visualize the capsule)
- Gram-positive, spore-forming rod

## » Gram stain morphology of *B. anthracis*:

- Broad, gram-positive rod: 1-1.5 x 3-5 μ occurring singly or in short chains, often with squared off ends
- Oval, central to subterminal spores: 1 x 1.5 μ with no significant swelling of cell
- Spores usually NOT present in clinical specimens unless exposed to atmospheric O<sub>2</sub>
- In advanced disease, a gram stain of unspun blood may be positive.

#### » Colonial and isolate characteristics of B. anthracis:

- After incubation on a blood agar plate for 15-24 hours at 35-37° C, well isolated colonies are 2-5 mm in diameter; heavily inoculated areas may show growth in 6-8 hours
- Gray-white, flat or slightly convex colonies are irregularly round, with edges that slightly undulate, and have "ground glass" appearance
- Often have comma-shaped protrusions from colony edge ("Medusa head" colonies)
- Tenacious consistency (when teased with a loop, stands up like a beaten egg white)
- Non-hemolytic (weak hemolysis may be observed under areas of confluent growth in aging cultures and should NOT be confused with real β-hemolysis)
- Non-motile
- Susceptible to gamma phage lysis

Detailed guidelines for testing for Bacillus anthracis are available on the CDC website at: <a href="https://www.bt.cdc.gov/Agent/Anthrax/LevelAProtocol/Anthracis20010417.pdf">www.bt.cdc.gov/Agent/Anthrax/LevelAProtocol/Anthracis20010417.pdf</a> or <a href="https://www.bt.cdc.gov">www.bt.cdc.gov</a>

# Risk assessment and response to possible anthrax exposures for clinicians

- Persons involved in an anthrax threat involving a letter or package with "powder" should report the incident immediately to the local law enforcement agency (911) for a threat assessment. The WA State Public Health Laboratory will only accept environmental samples for anthrax testing when law enforcement authorities, in consultation with Public Health, determine that a *credible threat* is present.
- Prophylactic antibiotics should be limited to persons with 1) potential aerosol exposure to a credible threat (as determined by law enforcement authorities in consultation with Public Health) and when no substance is available for testing, or 2) a confirmed anthrax exposure. Clinicians evaluating patients who may have been exposed to anthrax should have the patient report the incident immediately to local law enforcement (see above). If the clinician is concerned that a high-risk exposure (defined below) has occurred, please contact Public Health at 206-296-4774 (24 hours). Please consult with Public Health before starting anthrax post-exposure prophylaxis whenever possible.
- Detailed guidelines for handling suspicious packages, letters and substances can be found in the CDC Health Alert at: http://www.bt.cdc.gov/DocumentsApp/Anthrax/10122001Handle/10122001Handle.asp.

## » Assessment of individual risk of exposure:

- Factors that need to be assessed to define the nature of a possible exposure to anthrax include:
  - 1. The credibility of the threat (as determined by law enforcement and/or Public Health);
  - 2. Whether a potential human exposure occurred; and
  - 3. The specific circumstances of the exposure (e.g. risk of inhalational or cutaneous anthrax)
- Clinicians should take a thorough history from patients with illness compatible with anthrax
  including occupation, travel in the past 60 days, and circumstances of any exposure to
  suspicious substances.
- Situations with higher credibility for the presence of anthrax: a distinct threatening message is sent with the powder or substance, or a suspicious letter or package is involved (see the CDC Health Alert for details).
- Situations with lower credibility for the presence of anthrax: powder is found without a note or
  is present in an expected mail envelope or package that is easy to trace to the sender.

## » Route of potential exposure - based on information available as of 10-25-01:

Inhalational anthrax generally requires exposure to fine powder (1-5 microns in size) necessary to get into the alveoli. It is technically difficult to disperse anthrax into particles this size. Reaerosolization of particles deposited on clothing and other surfaces is thought to pose minimal to no risk. In the current anthrax attack on the Washington, DC area, the risk for aerosol exposure among persons exposed to anthrax powder in envelopes appears to be high. The risk of aerosol exposure would be expected to vary according to the specific characteristics of the anthrax preparation involved and the circumstances of exposure.

Inhalational anthrax would clearly be of concern with evidence of exposure to an aerosol of anthrax-contaminated powder. Examples include a fine powder contaminating the eyes, nose and throat; a credible threat or incident involving potential aerosolization based on information

regarding the circumstances of exposure, a warning that an air handling system is contaminated or a warning that a biological agent was released in a public space.

**Cutaneous anthrax** is the most likely form of anthrax that could be caused by anthrax-contaminated letters and packages that did not have an obvious aerosolizing device. Given the characteristic clinical presentation and excellent prognosis if recognized early and treated, potential cutaneous exposures that do not pose a risk for aerosol exposure can be managed by observation for the development of a suggestive skin lesion and prompt treatment as clinically needed.

## Management of persons with potential anthrax exposures

- DO NOT isolate the patient. Anthrax is not spread from person to person.
- There is *no need* to evacuate the immediate area.
- Provide support & understanding for patients, their families, and medical staff to prevent panic.
- Reinforce to patients the rarity of infection without known, confirmed culture-positive exposure.
- If exposed skin may have come in contact with an unknown substance/powder, recommend washing hands and showering with soap and water only.

## » Low Risk Exposure: report, reassure, refrain

- Definition: asymptomatic patient 1) WITHOUT known exposure to a confirmed culture-positive substance or credible threat associated with a letter, package or other scenario (as determined by law enforcement and Public Health); or 2) with exposure to a substance considered not to pose a credible threat by law enforcement authorities.
  - > Report to local law enforcement (911) if a potential threat exists and not already reported.
  - Reassure the patient about the low risk of infection in the absence of a confirmed culture-positive exposure.
  - ➤ Refrain from use of nasal swabs for diagnosis of exposure. Nasal swabs and blood serum tests are used as epidemiological tools to characterize an outbreak when there is a confirmed clinical case or exposure. Nasal swabs are not useful diagnostic tools for anthrax exposure in asymptomatic people.
  - Similarly, serologic studies that measure antibody titers to Bacillus anthracis are used as epidemiologic tools. Serologic tests are not indicated for screening or initial diagnostic purposes, and a single positive antibody titer is not diagnostic. To confirm an acute infection, seroconversion in an acute and convalescent serum must be documented.
  - Provide advice to the patient on the signs and symptoms of cutaneous and inhalational anthrax; reassure the patient that cutaneous anthrax can be readily diagnosed and treated.
  - Arrange for follow-up if indicated and if symptoms suggestive of anthrax develop.

## » High Risk Exposure: preventive treatment may be indicated

- Definition: asymptomatic patient with 1) potential aerosol exposure to a suspicious substance involving a credible threat (letter or other scenario) as determined by law enforcement authorities in consultation with Public Health; or 2) exposure to a substance confirmed to be positive for anthrax.
  - > Report to local law enforcement and Public Health if not already reported.
  - **Reassure** patient about the low risk of infection even with exposure to a confirmed, culture-positive environmental sample.
  - Hand washing and showering with soap and water are recommended, decontaminating the patient by means other than washing with soap and water is not indicated or recommended.
  - For confirmed anthrax exposures, see Tables at end of document for antibiotic prophylaxis guidelines.
  - ➢ If the situation suggests a true potential for aerosol exposure and 1) the threat is deemed credible by law enforcement and Public Health authorities and 2) no substance is available for testing, Public Health will issue recommendations for preventive therapy. In certain highly credible aerosol exposures, Public Health may recommend preventive therapy until anthrax has been ruled out by testing at the WA Public Health Laboratory and/or CDC.

# Management of suspicious substances and patients bringing suspicious substances to clinical facilities

- Do not panic.
- Call 911 and report the situation to local law enforcement.
- DO NOT shake or empty the contents of any suspicious package.
- DO NOT carry the package or envelope, show it to others, or allow others to examine
- Put the envelope or package on a stable surface; do not touch, sniff, taste, or look closely at it or any contents that may have spilled.
- All persons should leave the area, close any doors, and take actions to prevent others from entering the area. If possible, shut off the ventilation system.
- Remain on the premises and await instructions from law enforcement authorities and/or first responders.
- WASH hands carefully with soap and water to prevent powder from spreading to face or skin.
- If possible, list the names and contact information/telephone numbers for all people who were in the room or vicinity where the suspicious material was recognized.
   Provide this list to local first responders for follow-up investigations.
- For incidents involving possibly contaminated material, the environment in direct contact with the letter or its contents should be decontaminated with a solution of one part household bleach to 10 parts water, following a crime scene investigation.
   Personal effects may be decontaminated similarly.
- Patients should be instructed to shower with lots of soap and water as soon as possible. Do not use bleach or disinfectant on the skin.

## MMWR October 26, 2001 / 50(42);909-919 **Treatment Recommendations for Anthrax\***

\* Includes new recommendation for initiating multi-drug therapy for inhalational anthrax

TABLE 1. Inhalational anthrax treatment protocol\*.† for cases associated with this bioterrorism attack

Category	Initial therapy (intravenous) <sup>5,1</sup>	Duration
Adults	Ciprofloxacin 400 mg every 12 hrs* or Doxycycline 100 mg every 12 hrs <sup>††</sup> and One or two additional antimicrobials <sup>†</sup>	IV treatment initially**. Switch to oral antimicrobial therapy when clinically appropriate: Ciprofloxacin 500 mg po BID or Doxycycline 100 mg po BID
		Continue for 60 days (IV and po combined) <sup>55</sup>
Children	Ciprofloxacin 10–15 mg/kg every 12hrs ****  or  Doxycycline:****  >8 yrs and >45 kg: 100 mg every 12 hrs  >8 yrs and ≤45 kg: 2.2 mg/kg every 12 hrs  ≤8 yrs: 2.2 mg/kg every 12 hrs  and  One or two additional antimicrobials*	IV treatment initially**. Switch to oral antimicrobial therapy when clinically appropriate: Ciprofloxacin 10–15 mg/kg po every 12 hrs***  or Doxycycline:**  >8 yrs and >45 kg: 100 mg po BID  \$8 yrs and \$45 kg: 2.2 mg/kg po BID  Continue for 60 days (IV and po combined)**
Pregnant women <sup>sss</sup>	Same for nonpregnant adults (the high death rate from the infection outweighs the risk posed by the antimicrobial agent)	IV treatment initially. Switch to oral antimicrobial therapy when clinically appropriate. <sup>†</sup> Oral therapy regimens same for nonpregnant adults
Immunocompromised persons	Same for nonimmunocompromised persons and children	Same for nonimmunocompromised persons and children

- \* For gastrointestinal and oropharyngeal anthrax, use regimens recommended for inhalational anthrax.
- t Ciprofloxacin or doxycycline should be considered an essential part of first-line therapy for inhalational
- <sup>1</sup> Steroids may be considered as an adjunct therapy for patients with severe edema and for meningitis based on experience with bacterial meningitis of other etiologies.
- Other agents with in vitro activity include rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and clarithromycin. Because of concerns of constitutive and inducible beta-lactamases in Bacillus anthracis, penicillin and ampicillin should not be used alone. Consultation with an infectious disease
- specialist is advised.
  Initial therapy may be altered based on clinical course of the patient; one or two antimicrobial agents (e.g., ciprofloxacin or doxycycline) may be adequate as the patient improves.

  If meningitis is suspected, doxycycline may be less optimal because of poor central nervous system penetra-
- Because of the potential persistence of spores after an aerosol exposure, antimicrobial therapy should be continued for 60 days.
- If intravenous ciprofloxacin is not available, oral ciprofloxacin may be acceptable because it is rapidly and well absorbed from the gastrointestinal tract with no substantial loss by first-pass metabolism. Maximum serum concentrations are attained 1-2 hours after oral dosing but may not be achieved if vomiting or ileus are present.

  \*\*\* In children, ciprofloxacin dosage should not exceed 1 g/day.

  \*\*\*The American Academy of Pediatrics recommends treatment of young children with tetracyclines for serious infections (or a Papla Maymethia treatment).
- infections (e.g., Rocky Mountain spotted fever).
- Although tetracyclines are not recommended during pregnancy, their use may be indicated for life-threatening illness. Adverse effects on developing teeth and bones are dose related; therefore, doxycycline might be used for a short time (7-14 days) before 6 months of gestation.

## MMWR October 26, 2001 / 50(42);909-919 **Treatment Recommendations for Anthrax\***

\* Includes new recommendation for initiating multi-drug therapy for inhalational anthrax

TABLE 2. Cutaneous anthrax treatment protocol\* for cases associated with this bioterrorism attack

Category	Initial therapy (oral) <sup>†</sup>	Duration
Adults*	Ciprofloxacin 500 mg BID	60 days <sup>1</sup>
	or	
	Doxycycline 100 mg BID	
Children*	Ciprofloxacin 10–15 mg/kg every 12 hrs (not to exceed 1 g/day)†	60 days <sup>s</sup>
	or	
	Doxycycline: <sup>¶</sup>	
	>8 yrs and >45 kg: 100 mg every 12 hrs	
	>8 yrs and <45 kg: 2.2 mg/kg every 12 hrs	
	≤8 yrs: 2.2 mg/kg every 12 hrs	
Pregnant women*.**	Ciprofloxacin 500 mg BID	60 days <sup>s</sup>
	or	
	Doxycycline 100 mg BID	
Immunocompromised	Same for nonimmunocompromised persons	60 days <sup>s</sup>
persons*	and children	

\* Cutaneous anthrax with signs of systemic involvement, extensive edema, or lesions on the head or neck require intravenous therapy, and a multidrug approach is recommended. Table 1.

† Ciprofloxacin or doxycycline should be considered first-line therapy. Amoxicillin 500 mg po TID for adults or 80 mg/kg/day divided every 8 hours for children is an option for completion of therapy after clinical improvement. Oral amoxicillin dose is based on the need to achieve appropriate minimum inhibitory concentration levels.

<sup>1</sup> Previous guidelines have suggested treating cutaneous anthrax for 7-10 days, but 60 days is recommended in the setting of this attack, given the likelihood of exposure to aerosolized B. anthracis (6).

<sup>1</sup> The American Academy of Pediatrics recommends treatment of young children with tetracyclines for serious infections (e.g., Rocky Mountain spotted fever).

\*\* Although tetracyclines or ciprofloxacin are not recommended during pregnancy, their use may be indicated for life-threatening illness. Adverse effects on developing teeth and bones are dose related; therefore, doxycycline might be used for a short time (7–14 days) before 6 months of gestation.

TABLE 1. Interim recommendations for postexposure prophylaxis for prevention of inhalational anthrax after intentional exposure to Bacillus anthracis

Duration
60 days
* 60 days